

### **Remarks/Arguments**

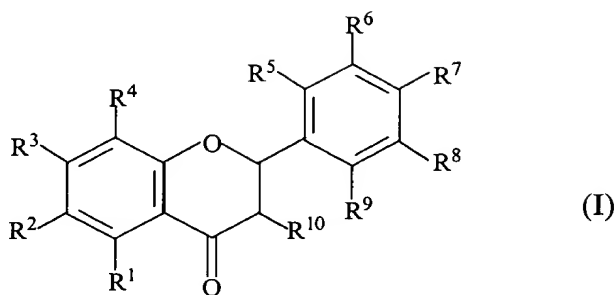
Claims 1-3 and 15-18 were pending in the application. Claim 1 has been amended to indicate that the extract is obtained by the method defined in the claim. The amendment is supported at page 5, lines 5-14. Claims 15, 17 and 18 are cancelled. Claim 16 is amended to depend from claim 1. New claims 19-22 have been added. The new claims are supported in the original claims as well as at page 3, line 7 to page 6, line 11; and page 7, line 4 to page 9, line 6. Claims 1-3, 16 and 19-22 are now pending in the application.

#### **Rejection Under 35 U.S.C. § 103(a)**

Claims 1-3 and 15-18 stand rejected under 35 U.S.C. § 103(a) as being obvious over GB 2,259,014 to Hadas et al. (hereinafter "Hadas") in view of U.S. Patent No. 3,598,841 to Swift (hereinafter "Swift"), JP 08-337,534 (hereinafter JP '534), and further in view of Machida et al., Chem. Pharm. Bull., Vol. 37, No. 4, pp. 1092-1094 (1989) (hereinafter "Machida") and Sarin et al., Tetrahedron, Vol. 8, pp. 64-66 (1960) (hereinafter "Sarin"). The Examiner suggests that it would have been obvious to make a composition according to Hadas employing Citrus unshiu extract because it is known as a whitening agent. Applicants respectfully disagree.

The present invention provides a cosmetic composition that includes:

(a) an extract obtained from a plant that is at least one of Citrus tachibana and Citrus unshiu comprising a polymethoxyflavone that is at least one compound represented by formula (I):



where each of  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ , and  $R^{10}$  is selected from the group consisting of hydrogen atom, hydroxyl group, alkoxy group having 1 to 20 carbon atoms, alkyl group having 1 to 20 carbon atoms, alkenyl group having 2 to 20 carbon atoms, hydroxyalkyl group having 1 to 20 carbon atoms or a sugar residue, and at least four of  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ , and  $R^{10}$  are methoxy groups;

(b) 0.01 to 10 wt % of a whitening agent selected from ascorbic acid and its salts or esters, kojic acid, hydroquinone, placental extracts, ellagic acid, and mixtures thereof; and

(c) the remainder being a base consisting essentially of water and at least one of ethanol, isopropyl alcohol, polyhydric alcohols, hydrocarbon oils, natural fats, natural oils, synthetic triglycerides, ester oils, waxes, polysiloxanes, oils, anionic surfactants, amphoteric surfactants, nonionic surfactants, cationic surfactants, semipolar surfactants, water soluble polymers, organic salts, inorganic salts, anti-inflammatory agents, pH regulators, germicidal agents, chelating agents, antioxidants, ultra violet absorbers, pigments, and fragrances.

The extract is obtained by a method that includes the steps of:

subjecting peel of a plant that is at least one of Citrus tachibana and Citrus unshiu to extraction with at least one solvent selected from methanol, ethanol,

propanol, butanol, ethyl acetate, acetone, propylene glycol and 1,3-butylene glycol to obtain an extract (S1);

dissolving the extract (S1) in ethyl acetate, adding water thereto, stirring, separating into layers, removing a water layer, and distilling off the ethyl acetate to obtain a dry solid product (S2); and

dissolving the dry solid product (S2) in a solvent, and subjecting it to liquid column chromatography.

Alternatively, the extract is obtained by a method that includes the steps of:

dissolving the extract (S1) in hexane and/or chloroform, removing a precipitate, distilling off the hexane and/or chloroform to obtain a dry solid product (S3); and

dissolving the dry solid product (S3) in a solvent, and subjecting it to liquid column chromatography.

The polymethoxyflavone is contained in an amount of 0.00005 to 10 wt % in the composition.

Thus, in amended claim 1 and new claim 19, the cosmetic composition of the present invention includes: (a) an extract obtained from at least one of Citrus tachibana and Citrus unshiu; the extract contains a polymethoxyflavone represented by a formula (I), in which at least four of ten substituents are methoxy groups; and the extract is obtained by a specific method as described in claims 1 or 19; (b) the polymethoxyflavone is contained in an amount of 0.00005 to 10 wt % in the composition; (c) a specific whitening agent; (d) the remainder.

Having such components (a) to (d), the cosmetic composition of the present invention can attain not only an excellent whitening effect to the skin but also a revitalizing of the skin and a suppressing of wrinkles and, furthermore, the composition has excellent storage stability.

By employing the method recited in claims 1 or 19, the obtained extract, which contains a specific amount of polymethoxyflavone, can contribute the effects of not only excellent storage stability of the composition but also revitalization of the skin and suppression of wrinkles as described above.

Hadas discloses a cosmetic composition for brightening skin comprising a flavonoid from plant or plant extract and an ascorbic acid. Hadas also discloses kojic acid as a whitening agent. However, Hadas discloses neither the specific polymethoxyflavone shown by formula (I) nor an amount of the polymethoxyflavone in a cosmetic composition. Further, Hadas does not disclose or suggest an extract which is obtained by a method as described in claims 1 or 19.

Swift discloses that Nobiletin, which is one of the polymethoxyflavones, is contained in an orange peel. Swift merely discloses a method for conversion of Tangeretin to Nobiletin, and therefore discloses neither a cosmetic composition comprising the specific polymethoxyflavone nor an amount of the polymethoxyflavone to be used in a cosmetic composition.

Machida discloses a method for purification of flavonoid from Citrus hassaku to obtain polymethoxyflavone. However, Machida does not disclose or suggest the method to obtain an extract from Citrus tachibana and Citrus unshiu of the present invention.

Sarin discloses a method for purification of flavonoid from Citrus aurantium to obtain polymethoxyflavone. However, Sarin does not disclose or suggest the method to obtain an extract from Citrus tachibana and Citrus unshiu of the present invention.

The Examiner takes the position that Hadas teaches a composition for skin whitening that includes a flavonoid and ascorbic acid or its derivatives; kojic acid enhances the whitening effect, and Swift discloses that citrus peels contain a significant amount of flavonoids employed herein.

However, Hadas does not teach or suggest the features of the present invention, that is, the presence of polymethoxyflavone represented by the formula (I), in which at least four of ten substituents are methoxy groups and the specific amount of polymethoxyflavone. Further, Hadas does not disclose or suggest the extract which is obtained by a method as described in claim 1 or claim 19.

Further, the Examiner alleges that since Swift teaches that citrus peels are known to contain significant amounts of flavonoids, and JP '534 teaches that the organic extract of Citrus unshiu is useful for whitening skin, a person of ordinary skill in the art would have been motivated to make a composition according to Hadas by employing the Citrus unshiu extract because Citrus unshiu extract is known to contain flavonoid and is known for the usefulness as a skin whitening agent.

However, since flavonoid is known to be distributed widely in plants as disclosed in Hadas, if a person of ordinary skill in the art seeks only the whitening effect using flavonoid, the person of ordinary skill in the art would select flavonoid without any limitation of source. As stated above, the purpose of the present invention is to provide a cosmetic composition that can attain not only an excellent

whitening effect to the skin but also revitalizes the skin and suppresses wrinkles and, furthermore, to produce compositions that have excellent storage stability. In order to obtain the added effects, over and above the whitening effect, it is necessary to employ an extract that contains a specific amount of flavonoid of Citrus unshiu or Citrus tachibana, where the extract is obtained by a specific method as recited in claims 1 or 19.

The combined cited prior art is silent to this advantage and provides no disclosure, direction or motivation for one skilled in the art as to how to obtain the whitening effect and skin revitalization effect as in the present claims.

None of Hadas, Swift and JP '534 discloses the use of the extract which contains a specific amount of flavonoid of Citrus unshiu or Citrus tachibana (components (a) and (b) above) that is prepared by a method as recited in claims 1 or 19 to obtain the above-mentioned effects. Hadas merely discloses the plant extract. Swift merely discloses the conversion of Tangeretin to Nobiletin. JP '534 merely discloses the use of an extract without any purification.

Since both Hadas and Swift are silent about the use of the extract of Citrus unshiu or Citrus tachibana prepared by a method as recited in claims 1 or 19 to obtain the effects other than whitening, a person of ordinary skill in the art would not have been motivated to combine Hadas and Swift.

Further, since JP '534 does not teach or suggest the amount of polymethoxyflavone in a cosmetic composition, the present invention would not have been obvious over Hadas in view of Swift and JP '534.

With respect to a method of preparing the extract, the Examiner takes the position that it would have been an obvious alternative to employ a purified or concentrated extract to a crude extract.

As the Examiner correctly points out, Machida and Sarin disclose purification of flavonoid and obtain polymethoxyflavones.

However, there are many potential steps to purify a desired compound. In the present invention, there are at least three steps required to obtain the extract. The first step is to extract the peel of Citrus unshiu or Citrus tachibana with a solvent (1) so as to obtain an extract (S1); the second step is to dissolve (S1) in ethyl acetate or hexane/chloroform followed by a specific separation process so as to obtain a solid dry product (S2) (claim 1) or (S3) (claim 19), respectively; and dissolving the solid dry product (S2) or (S3) in a solvent and subjecting it to liquid column chromatography.

Sarin discloses a quite different method compared with the present invention and, therefore, does not teach or suggest the use of the method or solvent used in the present invention.

Although Machida discloses the use of ethanol which is one of the solvents used to obtain the extract (S1) of the present invention, Machida does not teach or suggest the use of ethyl acetate as used in claim 1 and hexane/chloroform as used in claim 19 of the present invention.

There are many candidates of solvents to be used in the purification process. Therefore, it would not be possible for one of ordinary skill in the art to select ethyl acetate or hexane or chloroform from among the infinite number of

candidate solvents, because each of these three solvents has different characteristics in dissolving polymethoxyflavone.

In other words, the selection of the specifically claimed solvents could not be obtained without undue experimentation.

By using the claimed solvents and the claimed purification method, an extract that can provide the beneficial effects of excellent storage stability of the composition, revitalization of the skin and suppression of wrinkles is obtained, and such an extract contains a specific amount of polymethoxyflavone.

The Examiner alleges that it would have been an obvious alternative to employ a purified or concentrated extract to a crude extract.

However, since the selection of particular solvents in the purification process is important to exclude any undesired substances, it is well known to one of ordinary skill in the art that in order for the purified extract of the present invention to provide the various effects and benefits stated above, the selection of the solvent is a result of inventive efforts to discover unique extraction steps and specific solvent combinations from an infinite number of candidates. Therefore, it would not have been obvious to those skilled in the art to select a specific solvent in the first step and ethyl acetate (claim 1) or hexane/chloroform (claim 19) for extraction in the second step.

Further, the solvent system and the ratio of solvents in the solvent system used in column chromatography in claim 16 and 22, namely, hexane/ethanol v/v 70/30 to 97/3, are not disclosed or suggested by Machida and Sarin. As described, it is very difficult to identify and not at all obvious to select the combination of solvents and ratio of solvents in the present invention.



The Examiner alleges that, regarding the particular characteristics recited herein, the claiming of a new use, new function or unknown property, which is inherently present in the prior art, does not necessarily make the claim patentable.

However, because the extract of the present invention is different from the extract of Hadas, Swift and JP '534, and further different from that of Machida and Sarin as discussed above, the cosmetic composition of the present invention is new and the new properties such as excellent whitening effect to the skin, revitalizing the skin, suppressing wrinkles and having excellent storage stability are not inherent in the prior art.

Applicants have indicated that the cited references do not teach expressly the claimed process for obtaining the flavonoid from Citrus and, therefore, the claimed invention would not have been obvious over the cited references. The Examiner, in response, alleges that a particular process of isolating such flavonoid would not make the final product patentably distinct from the cited prior art, particularly in view of the fact that the process of isolating the flavonoid is a routine procedure similar to those disclosed in the cited prior art.

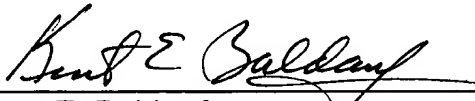
However, as stated above, the isolating method is not similar but clearly distinct from the cited prior art and, as a result, the obtained extract is quite different from that of the prior art. Therefore, the particular process of isolating flavonoid as in the present invention would make the final product patentably distinct over the cited prior art. Therefore, the present invention would not have been obvious over the prior art.

As stated above, claims 1-3, 16 and 19-22 would not have been obvious over Hadas in view of Swift and JP '534, and in further view of Machida and Sarin. Therefore, the rejection under 35 U.S.C. § 103(a) should be withdrawn.

In view of the above amendments and remarks, reconsideration of the rejections and allowance of claims 1-3, 16 and 19-22 are respectfully requested.

Respectfully submitted,

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